

## Advice on formaldehyde and glycol ethers



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26 scientists (see panel) met at the International Agency for Research on Cancer (IARC; Lyon, France) in June, 2004, to assess the carcinogenicity of formaldehyde and two glycol ethers to humans.<sup>1</sup> Formaldehyde is widely used in resins that bind wood products, pulp and paper; in glasswool and rockwool insulation; in plastics and coatings, textile finishing, chemical manufacture; and as a disinfectant and preservative.

Increased mortality from nasopharyngeal cancer has been reported in a cohort of US industrial workers,<sup>2</sup> and in two other cohort studies. Five of seven case-control studies showed that the carcinogenic risk was increased for people exposed to formaldehyde. The Working Group decided that it was, "improbable that all of the positive findings... could be explained by bias or by unrecognised confounding effects". They concluded that there is sufficient evidence that formaldehyde causes nasopharyngeal cancer in humans.

Increased deaths from leukaemia, especially myeloid, have been found in six of seven cohorts of embalmers, funeral-parlour workers, pathologists, and anatomists. These findings had previously been discounted because an increased incidence of leukaemia had not been seen in industrial workers. Recent updates, however, report a greater incidence of leukaemia in US industrial workers<sup>3</sup> and garment workers,<sup>4</sup> but not in chemical workers in the UK.<sup>5</sup> The Working Group concluded that there is, "strong but not

sufficient evidence for a causal association between leukaemia and occupational exposure to formaldehyde".

Several case-control studies have associated exposure to formaldehyde with sinonasal adenocarcinoma and squamous-cell carcinoma. However, analyses of updated cohorts<sup>2,4,5</sup> have not reported increased incidence of sinonasal cancer. The Working Group concluded that there is limited evidence that formaldehyde causes sinonasal cancer in humans.

Inhalation studies in rats have shown that formaldehyde induces squamous-cell carcinoma of the nasal cavity. Four studies in which formaldehyde was given in the rats' drinking water gave mixed results, whereas formaldehyde had cocarcinogenic effects when inhaled, ingested, or applied to the skin.

Studies in vitro, in animals, and in humans have shown that formaldehyde is genotoxic. Increased numbers of DNA-protein crosslinks have been found in exposed workers—similar to results found in animal studies. Cell proliferation increases substantially at formaldehyde concentrations higher than six parts per million, amplifying the genotoxic effect. The Working Group concluded that, "both genotoxicity and cytotoxicity have important roles in the carcinogenesis of formaldehyde in nasal tissues". By contrast, the Working Group could not identify a mechanism for leukaemia induction.

Overall, the Working Group concluded that formaldehyde is "carcinogenic to humans", on the basis of sufficient evidence in humans and animals—a higher classification than previous IARC assessments.

2-butoxyethanol is a glycol ether widely used as a solvent in paints and paint thinners, glass and surface cleaners, personal-care products, and as a chemical intermediate. An inhalation study<sup>6</sup> by the US National Toxicology

## Upcoming meetings

Oct 5–12, 2004 Smokeless tobacco and related nitrosamines

Feb 15–22, 2005 Human papillomaviruses

Program (NTP) found liver haemangiosarcoma in male mice, forestomach squamous-cell papilloma and carcinoma in female mice, and equivocal results in female rats. An association between haemolysis and liver neoplasia in mice has been suggested, but the Working Group noted that other potential mechanisms have not been investigated. 1-tert-butoxy-2-propanol is a glycol ether used as a solvent in coatings, glass and surface cleaners, inks, adhesives, and nail-polish lacquers. An NTP inhalation study<sup>7</sup> found liver tumours, including hepatoblastoma, in mice and equivocal results in male rats.

The Working Group concluded that 2-butoxyethanol and 1-tert-butoxy-2-propanol are "not classifiable" because of limited evidence in animals and inadequate evidence in humans.

## References

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- 6 US National Toxicology Program. Toxicology and carcinogenesis studies of 2-Butoxyethanol (CAS No 111-76-1) in F344/N rats and B6C3F1 mice (inhalation studies). Triangle Park: NTP TR 484, NIH Pub No 00-3974, 2000.
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